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EXAMINER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DENIS GARCEAU,
WENDY HAUCK, and RICHARD BRIAND¹

Appeal 2016-002134
Application 13/901,432
Technology Center 1600

Before FRANCISCO C. PRATS, JOHN E. SCHNEIDER, and
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134(a) involves claims to methods of treating AA amyloidosis. The Examiner rejected the claims for obviousness.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The Specification discloses that “[a]myloidosis is the generic term for a number of diseases related by extracellular deposition of insoluble fibrillar proteins (amyloid) in specific organs, which eventually leads to the failure of the involved organs.” Spec. 1. “Systemic amyloidoses are generally

¹ Appellants state that the “real party in interest in this patent application is Kiacta Sàrl.” Br. 3.

classified into four types based on the nature of the fibrillar deposits: (i.) idiopathic or primary amyloidosis (AL amyloidosis); (ii.) reactive, secondary or amyloid A (AA) amyloidosis; (iii.) familial amyloidotic polyneuropathy; and (iv.) dialysis-associated amyloidosis.” Spec. 1.

“Generally, AA amyloidosis is a manifestation of a number of diseases that provoke a sustained acute phase response. Such diseases include chronic inflammatory disorders, chronic local or systemic microbial infections, and malignant neoplasms.” *Id.* at 12.

Claim 14, the sole independent claim on appeal, illustrates the appealed subject matter and reads as follows:

14. A method of treating AA amyloidosis associated with a chronic infection in a subject in need thereof, said method comprising:

administering to said subject a therapeutically effective amount of

1,2-ethanedisulfonic acid,
sodium 1,2-ethanedisulfonate,
1,3-propanedisulfonic acid, or
sodium 1,3-propanedisulfonate (1,3-propanedisulfonic acid, disodium salt),

in combination with a second agent such that the chronic infection is treated in said subject.

The following rejections are before us for review:

(1) Claims 7, 8, and 14, under 35 U.S.C. § 103(a), for obviousness over Garceau² and Castellano³ (Ans. 2–4); and

² Denis Garceau et al., *A prospective analysis of demography, etiology, and clinical findings of AA amyloidosis patients enrolled in the international clinical Phase II/III FibrillexTM study* (slide presentation) (2004) (publication date provided in information disclosure statement entered March 25, 2014).

(2) Claims 3 and 4, under 35 U.S.C. § 103(a), for obviousness over Garceau, Castellano, and Kisilevsky⁴ (Ans. 4–5).

OBVIOUSNESS—
GARCEAU AND CASTELLANO

The Examiner's Rejection

The Examiner cites Garceau as disclosing “the treatment of AA amyloidosis associated with a chronic infection like tuberculosis, osteomyelitis, etc. comprising the administration of 1,3-propanedisulfonate (also known as Fibrillex TM, Eprosdate or NC-503).” Ans. 2 (emphases and citation omitted).

The Examiner finds that Garceau differs from the rejected claims in that “Garceau does not teach the administration of a second agent such that the chronic infection (i.e. tuberculosis) is treated in said subject.” *Id.* at 3.

To address that deficiency, the Examiner cites Castellano as teaching that “secondary systemic amyloidosis (AA amyloidosis) is a frequent complication of different chronic infectious disorders like for example tuberculosis” and “that treatment of tuberculosis with agents like: rifampicin, pyrazinamide and/or isoniazid in patients having AA amyloidosis associated with tuberculosis causes a remission of AA amyloidosis.” *Id.* (emphases and citation omitted).

Based on the references' teachings, the Examiner concludes that an ordinary artisan would have considered it obvious “to treat a subject suffering from tuberculosis and AA amyloidosis associated with tuberculosis

³ I. Castellano et al., *Remission of Nephrotic Syndrome Caused By Renal Amyloidosis Secondary to Pulmonary Tuberculosis after Tuberculostatic Treatment*, 21 Nefrología 88–91 (2001) (as translated).

⁴ US 5,643,562 (issued July 1, 1997).

with two agents that separately treat both diseases (tuberculosis and AA amyloidosis associated with tuberculosis)” Ans. 3 (emphases omitted).

In particular, the Examiner reasons:

[I]t would have been *prima facie* obvious for a person of ordinary skill in the art to treat AA amyloidosis associated with tuberculosis (a chronic infection) combining two compositions (1,3-propanedisulfonic acid or its sodium salts and agents that treat tuberculosis like: rifampicin, pyrazinamide and/or isoniazid) each of which is taught by the prior art to be useful for the same purpose (treating AA amyloidosis associated with tuberculosis), in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Analysis

As stated in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992):

[T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. . . .

After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

In the present case, Appellants do not persuade us that a preponderance of the evidence fails to support the Examiner’s conclusion of obviousness.

Appellants’ claim 14 recites a method of treating AA amyloidosis associated with a chronic infection. Br. 15. Claim 14 requires administering two agents: (1) “1,2-ethanedisulfonic acid, sodium 1,2-ethanedisulfonate, 1,3-propanedisulfonic acid, or sodium 1,3-propanedisulfonate

(1,3-propanedisulfonic acid, disodium salt), in combination with [(2)] a second agent such that the chronic infection is treated” Br. 15.

As the Examiner finds, Garceau discloses a Phase II/III study of the treatment of AA amyloidosis with Fibrillex, which Appellants do not dispute is 1,3-propanedisulfonate, and which Appellants do not dispute is one of the first group of ingredients recited in claim 14. *See* Garceau 1.⁵ As the Examiner finds, Garceau discloses that pulmonary tuberculosis is among the underlying diseases in the treated AA amyloidosis patients. *Id.* at 9.

Like Garceau, Castellano discloses that “[s]econdary systemic amyloidosis (AA amyloidosis) is a frequent complication of different infectious chronic disorders. In the first descriptions of the disease, the pathologies that were more often associated with AA amyloidosis were infections, especially tuberculosis, syphilis and osteomyelitis.” Castellano 1 (citations omitted).

Castellano discloses the treatment of a subject with AA amyloidosis, accompanied by tuberculosis, with several therapeutic agents:

We report the case of a woman of 16 years who develops nephrotic syndrome one month after the diagnosis of pulmonary tuberculosis. Biopsy shows the existence of renal amyloidosis. Receives TB treatment for 12 months, and two years later enters into remission of the nephrotic syndrome. . . . In 1991 admitted to our hospital with a woman 16 years for lower limb edema and sacrum 36 hours of evolution. Ten months earlier, had presented a general discomfort with anorexia, asthenia and fever, being diagnosed one month before admission with pulmonary tuberculosis by AFB and sputum

⁵ The Garceau reference does not include page numbers. We cite to the first page of the reference as page 1, and the remaining pages as if numbered consecutively.

culture and bronchial amid Lowenstein, and initiating treatment rifampicin (480 mg/24 hours), pyrazinamide (1200 mg/24 hours) and isoniazid (200 mg/24 hours).

Castellano 1.

Thus, although neither Garceau, nor Castellano describes treating a patient using the specific combination of agents required by Appellants' claim 14, an ordinary artisan would have been advised by Garceau that Fibrillex was useful for treating AA amyloidosis associated with an underlying tuberculosis infection, and further advised by Castellano that using a plurality of therapeutic agents, including rifampicin, pyrazinamide, and isoniazid, was useful for treating AA amyloidosis associated with a chronic tuberculosis infection. Given these teachings, we agree with the Examiner that an ordinary artisan had ample reason for, and a reasonable expectation of success in, combining Garceau's therapeutic agent with any of the agents taught in Castellano, for the treatment of AA amyloidosis associated with a chronic tuberculosis infection. Accordingly, we agree with the Examiner that the process recited in claim 14 would have been *prima facie* obvious to an ordinary artisan.

Appellants' arguments do not persuade us to the contrary.

Appellants contend that, "[e]ven if the Examiner's characterization of Castellano is accurate, the potential coexistence of two indications is no guarantee that agents which address such indications will be compatible with one another, will not operate by competing mechanisms of action, etc." Br.

12. Appellants contend further:

Only the present Appellants recognize the compatibility and the utility of the specific combination required by the present claims for the treatment of a defined condition (*i.e.*, AA

amyloidosis associated with a chronic infection) in a subject in need thereof, i.e., a therapeutically effective amount of:

a compound selected from a defined group of alkyl sulfates/sulfonates, and

a second agent such that the chronic infection is treated in said subject.

Br. 12.

As our reviewing court has explained, however, obviousness “does not require absolute predictability of success. . . . For obviousness under § 103, all that is required is a reasonable expectation of success.” *In re O’Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988); *accord*, *In re Kubin*, 561 F.3d 1351, 1359–61 (Fed. Cir. 2009).

In the present case, as noted above, Castellano discloses that the therapeutic agents it used were amenable to use in a combination therapy. Appellants do not persuade us, therefore, that an ordinary artisan lacked a reasonable expectation that other therapeutic agents known for use in treating AA amyloidosis associated with an underlying tuberculosis infection, such as Garceau’s Fibrillex, would have been incompatible with Castellano’s therapeutic agents. Appellants, moreover, do not advance any specific persuasive evidence suggesting that Fibrillex would have been expected to be incompatible with other drugs in general, or Castellano’s therapeutic agents in particular.

In sum, for the reasons discussed, Appellants do not persuade us that the evidence of record fails to support the Examiner’s *prima facie* case of obviousness as to claim 14. Appellants, moreover, do not advance secondary evidence of nonobviousness to rebut the Examiner’s *prima facie* case. Accordingly, because a preponderance of the evidence supports the Examiner’s conclusion of obviousness as to claim 14, we affirm the

Examiner's rejection of that claim over the cited references. Because they were not argued separately, claims 7 and 8 fall with claim 14. 37 C.F.R. § 41.37(c)(1)(iv).

OBVIOUSNESS—
GARCEAU, CASTELLANO, AND KISILEVSKY

Claim 3 recites “[t]he method of claim 14 wherein said compound is 1,2-ethanedisulfonic acid.” Br. 15.

Claim 4 recites “[t]he method of claim 14 wherein said compound is sodium 1,2-ethanedisulfonate.” *Id.*

In rejecting claims 3 and 4, the Examiner relied on the teachings in Garceau and Castellano discussed above, and cited Kisilevsky as evidence that 1,2-ethanedisulfonic acid and sodium 1,2-ethanedisulfonate were known in the art to be equivalently useful to Garceau's agent for treating AA amyloidosis. *See* Ans. 4. The Examiner concluded, therefore, that it would have been obvious to substitute 1,2-ethanedisulfonic acid or sodium 1,2-ethanedisulfonate for Garceau's agent when treating AA amyloidosis. *Id.* at 4–5.

Appellants do not allege error in the Examiner's characterization of Kisilevsky. Rather, Appellants contend:

Further reliance on Kisilevsky is unable to cure the acknowledged deficiencies of the combination of Garceau and Castellano since Kisilevsky is merely relied upon for the proposition that 1,3-propanedisulfonic acid is a functional equivalent of 1,2-ethanedisulfonic acid—thus adding nothing to the consideration of whether there is any motivation in the art to combine 1,2-ethanedisulfonic acid (or 1,3-propanedisulfonic acid) with any second agent, much less a second agent such that the chronic infection is treated in said subject. Moreover, the combination of Garceau and Castellano with Kisilevsky provides no expectation that such a combination would be

compatible and, if so, would also be functional for the intended purpose.

Br. 13. We are not persuaded.

In particular, for the reasons discussed above, we are not persuaded that the combination of Garceau and Castellano is deficient in establishing a reason for, and a reasonable expectation of success in, combining the therapeutic agents taught in those references. Moreover, given Castellano's disclosure that the therapeutic agents it used were amenable to use in a combination therapy, we agree with the Examiner that an ordinary artisan also had a reasonable expectation that 1,2-ethanedisulfonic acid and sodium 1,2-ethanedisulfonate, undisputedly taught in Kisilevsky as being useful for treating AA amyloidosis, would also be compatible with Castellano's agents when treating that disorder.

SUMMARY

For the reasons discussed, we affirm each of the Examiner's rejections.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED